REMARKS

The Present Invention

The present invention pertains to nucleic acid molecules, compositions comprising the same, a recombinant expression vector, a host cell comprising the same, a method for detecting a nucleic acid encoding Rig, and a method for amplifying a nucleic acid encoding Rig.

The Pending Claims

Claims 1-4, 6-16, and 29-39 are pending of which claims 1-3 are directed to a recombinant expression vector, claim 4 is directed to a host cell comprising the same, claims 6-10 are directed to a method of detecting a nucleic acid encoding Rig, claims 11-16 and 29 are directed to a method of amplifying a nucleic acid encoding Rig, claims 30, 31, 33, 35, and 38 are directed to nucleic acid molecules, claims 32, 34, 37, and 39 are directed to compositions comprising the same, and claim 36 is directed to a host cell comprising a nucleic acid molecule.

The Final Office Action

The Office has maintained the rejection of claims 6-16 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement, and further rejects claim 29 on the same basis. The Office also has maintained the rejection of claims 6-16 and 29 under 35 U.S.C. § 112, first paragraph, as allegedly lacking a written description, and further rejects claim 29 on the same basis. Claim 3 has been rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. The Office has maintained the rejection of claims 6-16 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. The Office has maintained the rejection of claims 1 and 4 under 35 U.S.C. § 102 (b) as allegedly anticipated by Lamerdin et al., GenBank Accession No. AC006538 (herein referred to as Lamerdin et al.). The Office has maintained the rejection of claims 6-15 under 35 U.S.C. § 102(b) as allegedly anticipated by Yu et al., *P.N.A.S.* 96: 214-219 (1999) (herein referred to as Yu et al.), and further rejects claim 29 on the same basis. The Office has maintained the rejection of claims 1 and 2 under 35 U.S.C. § 103 (a) as allegedly *prima facie* obvious in view of Lamerdin et al. The Office has maintained the rejection of claims 1, 3 and 4 under 35 U.S.C. § 103 (a) as allegedly *prima facie* obvious in view of Lamerdin et al., Kimmelman et al., *Oncogene* 15: 2675-2685 (1997) (herein referred to as Kimmelman et al.), U.S. Patent No. 6,077,686 (herein referred to as the '686 patent), and

Baker et al., *Nucleic Acids Res.* 25: 1950-1956 (1997) (herein referred to as Baker et al.). The Office has maintained the rejection of claims 1, 6-11 and 13-15 under § 103 (a) as allegedly *prima facie* obvious in view of Lamerdin et al. in combination with Kimmelman et al., and further rejects claim 29 on the same basis. The Office also has maintained the rejection of claim 12 under § 103 (a) as allegedly *prima facie* obvious in view of Lamerdin et al. in combination with Kimmelman, U.S. Patent No. 4,695,188 (herein referred to as the '188 patent), and U.S. Patent No. 5,981,183 (herein referred to as the '183 patent). The Office has maintained the rejection of claim 15 under 35 U.S.C. § 103 (a) as allegedly obvious in view of Lamerdin et al. in combination with Kimmelman et al. and the '188 patent. The Office also has maintained the rejection of claim 16 under 35 U.S.C. § 103 (a) as allegedly *prima facie* obvious in view of Lamerdin et al. in combination with Kimmelman et al., U.S. Patent No. 5,314,809 (herein referred to as the '809 patent), and U.S. Patent No. 5,397,703 (herein referred to as the '703 patent). Reconsideration of these rejections is hereby requested.

Amendments to the Claims

Claim 3 was previously amended to recite "is" in lieu of "further comprises" (see page 7, line 16 of the Amendment and Response to Office Action, mailed July 25, 2003). Applicants hereby request that this amendment be entered. The preamble of each of claims 6 and 11 has been amended to recite "a Rig protein (SEQ ID NO: 5)." Claims 30-33 have been added, of which claims 30-34 are supported by the specification at, for instance, Figure 1, page 11, lines 1-7, page 21, line 19, through page 22, line 25, page 10, lines 13 and 14, page 12, line 25, through page 13, line 5, and page 4, line 29. Claims 35-39 are supported in the specification at, for instance, page 11, lines 1-7, page 15, line 24, through page 16, line 8, page 21, line 19, through page 22, line 25, page 4, line 29, page 32, lines 16-23, page 12, line 25, though page 13, line 5, and Examples 5, 7, 8, and 10. No new matter has been added by way of these amendments.

Discussion of the Indefiniteness Rejection

Claim 3 has been rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Specifically, the Office contends that claim 3 lacks a verb. This rejection is traversed, since claim 3 was previously amended to recite "is" in lieu of "further comprising" in the Amendment and Response to Office Action, mailed July 25, 2003 (see page 7, line 16). Therefore, this rejection is believed to be moot.

The Office has maintained the rejection of claims 6-16 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Specifically, the Office argues that the recitation of "Rig" is unclear. This rejection is traversed for the reasons set forth below.

The Manual of Patent Examining Procedure (MPEP) states the following:

The meaning of every term used in any of the claims should be apparent from the descriptive portion of the specification with clear disclosure as to its import (Section 608.01 (o)).

The meaning of every term used in a claim should be apparent from the prior art or from the specification and drawings at the time the application is filed (Section 2173.05 (a)).

As stated in the last Amendment and Response to Office Action, mailed July 25, 2003, the specification is replete with guidance as to what is meant by the term "Rig." For instance, the specification at page 4, lines 27 and 28, teaches that Rig stands for "Ras-related Inhibitor Gene" and that the Rig protein is a member of the Ras protein family and has tumor-suppressing activity. The specification further teaches the Rig amino acid sequence (SEQ ID NO: 5) and a cDNA sequence encoding the Rig protein (SEQ ID NO: 4). Further taught by the specification is the tissue expression pattern of Rig (Figure 4), the tumor expression pattern of Rig (Figure 5), the focus formation-inhibiting activity of Rig (Figures 6 and 8), the ability of Rig to bind to Raf-1 (Figure 9), and the ability of Rig to inhibit tumor growth (Figure 10). Given all of these teachings of the Rig protein, one of ordinary skill in the art would be able to make a determination as to what is and is not a Rig protein.

The Office further alleges that Applicant has failed to point to any limiting definition of the term "Rig" that would distinguish Rig from any other Ras-related inhibitor gene. However, Figure 1 of the instant specification and the corresponding description thereof (page 8, lines 1-6) teach the nucleotide sequences of the Rig gene and the amino acid sequence of Rig. Figure 2 of the instant specification teaches that Rig differs in amino acid sequence from other Ras proteins.

The Office also contends that the specification does not teach the minimal functional requirements of a Rig protein. Applicants respectfully submit that one of ordinary skill in the art, upon reading the specification in its entirety, would understand that a Rig protein is a protein that meets all of the functional characteristics described in the specification. There is no indication in the specification that a Rig protein is intended to encompass a protein that does not have a particular characteristic of Rig as set forth in the instant specification.

In order to advance prosecution and not in acquiescence of the rejection, however, the preamble of each of claims 6 and 11 has been amended to recite "a Rig protein (SEQ

ID NO: 5)" to make clear that by the term "Rig" is meant the protein having the amino acid sequence of SEQ ID NO: 5. In view of these amendments, this rejection is believed to be moot.

Discussion of the Lack of Enablement Rejection

The Office has maintained the rejection of claims 6-16 under Section 112, first paragraph, as allegedly lacking enablement, and further rejects claim 29 on the same basis. This rejection is traversed for the reasons set forth below.

The Office specifically contends that the specification is not enabling for methods of detecting or amplifying a nucleic acid encoding a Rig polypeptide other than the nucleic acid having the nucleotide sequence of SEQ ID NO: 5, namely because the term "Rig polypeptide" renders the scope of the claims unclear. However, as discussed in the last Amendment and Response to Office Action (mailed July 25, 2003) and as discussed above, one of ordinary skill in the art is, in fact, able to make a determination as to what is and is not a Rig protein, given all of the teachings on the Rig protein in the specification. Furthermore, one of ordinary skill in the art is enabled to test a given nucleic acid molecule to see if it encodes a Rig polypeptide. The specification, moreover, teaches how to detect a nucleic acid encoding a Rig polypeptide at, for instance, page 45, line 6, through page 46, line 18, and page 79, line 17, through page 80, line 15, and teaches how to amplify a nucleic acid encoding a Rig polypeptide at, for example, page 17, line 15, through page 18, line 27, and page 78, lines 7-19.

However, in order to advance prosecution and not in acquiescence of the rejection, the preamble of each of claims 6 and 11 has been amended to recite "a Rig protein (SEQ ID NO: 5)." In view of these amendments, this rejection is believed to be moot.

Discussion of the Lack of Written Description Rejection

The Office has maintained the rejection of claims 6-16 under 35 U.S.C. 112, first paragraph, as allegedly lacking a written description, and further rejects claim 29 on the same basis. This rejection is traversed for the reasons set forth below.

The Office specifically contends that the scope of the claims is unclear, as the specification fails to give an adequate definition of what is and what is not a Rig polypeptide. The Office further argues that it is unclear as to whether or not the 8 Ras-related polypeptides disclosed in the specification are considered Rig polypeptides. However, as discussed in the last Amendment and Response to Office Action and as discussed above, one of ordinary skill in the art is able to make a determination as to what

is and is not a Rig protein, given all of the teachings on the Rig protein in the specification. Also, as the specification teaches that the Rig protein is predicted to have the amino acid sequence of SEQ ID NO: 5 (see Figure 1, for example) and since the 8 Ras-related polypeptides disclosed in the specification have different amino acid sequences, it is clear to one of ordinary skill in the art that the 8 Ras-related polypeptides are not considered to be the Rig protein.

However, in order to advance prosecution and not in acquiescence of the rejection, the preamble of each of claims 6 and 11 has been amended to recite "a Rig protein (SEQ ID NO: 5)." In view of these amendments, this rejection is believed to be moot.

Discussion of the Anticipation Rejection

The Office has maintained the rejection of claims 1 and 4 under Section 102 (b) as allegedly anticipated by Lamerdin et al. This rejection is traversed for the reason set forth below.

The Office specifically contends that Lamerdin et al. discloses a bacterial artificial chromosome (BAC) comprising 177 kb of human chromosome 19, including a segment encoding the amino acid sequence of SEQ ID NO: 5, and 105 kb of upstream genomic sequence. The Office concludes that "it is clear that this nucleic acid comprises the transcriptional control elements for this open reading frame. For this reason, the bacterial artificial chromosome...is an expression vector for SEQ ID NO: 5" (see page 14 of Paper No.13). Furthermore, in response to the introduction of the phrase "consisting essentially of" in claim 1, the Office states that Applicant has provided no evidence or argument that the BAC of Lamerdin et al. materially affects the basic and novel characteristics of the claimed invention in any way, and the specification provides no indication of what is essential to the basic and novel characteristics of the claimed invention.

As the Office knows, the term "consisting essentially of" limits the scope of a claim to the specified materials or steps (MPEP § 2111.03). Claim 1 specifies that the recombinant expression vector consists essentially of an open reading frame encoding SEQ ID NO: 5 and one or more regulatory elements. Since Lamerdin et al. discloses over 177 kilobasepairs, parts of which encode at least 9 other predicted exons and at least 2 other proteins, Lamerdin et al. discloses other nucleic acid sequences that one of ordinary skill in the art would recognize as sequences that would materially affect the subject inventive recombinant expression vector. In this regard, Lamerdin et al. does not anticipate claim 1. As claim 4 depends on claim 1, Lamerdin et al. also does not

anticipate claim 4. Applicants, therefore, request that the anticipation rejection of claims 1 and 4 be withdrawn.

The Office also has maintained the rejection of claims 6-15 under Section 102 (b) as allegedly anticipated by Yu et al., and further rejects claim 29 on the same basis. This rejection is traversed for the reasons set forth below.

The Office specifically alleges that Yu et al. discloses detection of a poly mRNA from human tumor tissue of a nucleic acid encoding Noey2, a polypeptide that is 63% identical to SEQ ID NO: 5. The Office further asserts that Yu et al. discloses identification of a Noey2 gene in genomic DNA. The Office concludes that, because the specification allegedly does not exclude Noey2 from the genus of polypeptides that may be construed as a Rig polypeptide, Yu et al. anticipates a method of detecting nucleic acids encoding Rig in a sample. However, as stated above, the teachings of the specification make it clear to one of ordinary skill in the art that a Rig protein has the amino acid sequence of SEQ ID NO: 5 (See, for example, Figure 1). Therefore, because Yu et al. does not disclose a polypeptide of SEQ ID NO: 5, Yu et al. does not anticipate the present inventive methods of detecting or amplifying a nucleic acid encoding a Rig protein. Furthermore, because the preamble of each of claims 6 and 11 has been amended to recite "a Rig protein (SEQ ID NO: 5)," this rejection is believed to be moot.

Discussion of the Obviousness Rejections

The Office has maintained the rejection of claims 1 and 2 under Section 103 (a) as allegedly *prima facie* obvious in view of Lamerdin et al. The Office also has maintained the rejection of claims 1, 3, and 4 under Section 103 (a) as allegedly *prima facie* obvious in view of Lamerdin et al. in combination with Kimmelman et al., the '686 patent; and Baker et al. The Office has maintained the rejection of claims 1, 6-11, and 13-15 under Section 103 (a) as allegedly *prima facie* obvious in view of Lamerdin et al. in combination with Kimmelman et al., and further rejects claim 29 on the same basis. The Office has maintained the rejection of claim 12 under Section 103 (a) as allegedly *prima facie* obvious in view of Lamerdin et al. in combination with Kimmelman et al. and the '188 and '183 patents. The Office also has maintained the rejection of claim 15 under Section 103 (a) as allegedly *prima facie* obvious in view of Lamerdin et al. in combination with Kimmelman et al. and the '188 patent. Finally, the Office has maintained the rejection of claim 16 under Section 103 (a) as allegedly *prima facie* obvious in view of Lamerdin et al. in combination with Kimmelman et al. and the '809 and '703 patents. These rejections are traversed for the reasons set forth below.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion of motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). [MPEP § 2143]. Because the references cited by the Office, alone or in combination with one another, do not teach or suggest each and every element of the rejected claims, the subject matter of these claims is not obvious.

With respect to the obviousness rejections of claims 1 and 2, Applicants previously argued in the last Amendment and Response to Office Action that Lamerdin et al. does not teach a recombinant expression vector consisting essentially of an open reading frame encoding SEQ ID NO: 5 operably linked to one or more regulatory elements. The Office specifically alleges that Applicant's previous argument is not persuasive, since Lamerdin et al. discloses a BAC, which is a recombinant expression vector. However, the Office is failing to recognize that claim 1 recites the transitional phrase "consisting essentially of" and, as stated above, Lamerdin et al. discloses over 177 kilobasepairs, parts of which encode at least 9 other predicted exons and at least 2 other proteins. In this regard, Lamerdin et al. discloses other nucleic acid sequences that one of ordinary skill in the art would recognize as sequences that would materially affect the subject inventive recombinant expression vector. Therefore, contrary to what the Office asserts on page 25 of Paper No. 15, Lamerdin et al. does not disclose a recombinant expression vector that *consists essentially of* an open reading frame encoding SEQ ID NO: 5. In this respect, Lamerdin et al. does not render the subject matter of claim 1 or any claim dependent thereon (claims 2-4) obvious.

With respect to the obviousness rejection of claims 1, 3, and 4, and in view of the foregoing argument, Lamerdin et al. in combination with Kimmelman et al., the '686 patent, and Baker et al., do not render the subject matter of claims 1, 3, and 4 obvious, since none of Kimmelman et al., the '686 patent, and Baker et al. cure the deficiency of Lamerdin et al., i.e., none teach a recombinant expression vector *consisting essentially of* an open reading frame encoding SEQ ID NO: 5 operably linked to one or more regulatory elements.

With respect to the obviousness rejection of claims 1, 6-11, 13-15, and 29, because

Kimmelman et al. does not cure the deficiency of Lamerdin et al., the combination of Kimmelman et al. and Lamerdin et al. does not render the subject matter of claim 1 obvious to one of ordinary skill in the art. Furthermore, since claims 6 and 11 read on "SEQ ID NO: 4" and because neither Lamerdin et al. nor Kimmelman et al. teaches SEQ ID NO: 4, the combination of Lamerdin et al. and Kimmelman et al. does not render the subject matter of claims 6 and 11, as well as any claims dependent thereon, obvious to one of ordinary skill in the art.

With respect to the obviousness rejections of claim 12, 15, and 16, since each of these claims depend on claim 11, and because claim 11 reads on SEQ ID NO: 4, which is neither taught nor suggested by any of Lamerdin et al., Kimmelman et al., or any of the '188, '183, '809, and '703 patents, the combination of any of these references cannot be said to render obvious the subject matter of claims 12, 15, or 16.

With regard to the rejection of claims 1 and 2, the Office alleges that Applicants did not address the issue of whether or not it would have been obvious to substitute a CAA codon for a CAG codon. However, claim 1 is directed to a recombinant expression vector consisting essentially of an open reading frame encoding SEQ ID NO: 5, which is an amino acid sequence. Thus, whether or not it was obvious to make the substitution is immaterial, since the claim does not read on any particular nucleotide sequence.

With regard to the rejection of claims 1, 3, and 4, the Office asserts that Applicants did not argue that there would be no motivation to remove the open reading frame of Lamerdin et al. from the BAC and transfer it to the cited recombinant expression vectors. Although Applicants believe that there is no teaching or suggestion in the relevant art to remove the open reading frame of Lamerdin et al. from the BAC and transfer it to a recombinant expression vector, this point is immaterial in light of the fact that Lamerdin et al. does not teach or suggest a recombinant expression vector *consisting essentially of* an open reading frame encoding SEQ ID NO: 5, as argued above.

With respect to the rejection of claims 6-16 and 29, the Office contends that Applicant presented no evidence or argument that the nucleic acid of Lamerdin et al. did not encode SEQ ID NO: 5, that there would be no motivation to use the nucleic acid as a probe to detect nucleic acids, or that these target nucleic acids would not encode some species of Rig. Furthermore, the Office argues that Applicants presented no evidence or argument that one would not have been motivated to amplify the nucleic acid of Lamerdin et al. as discussed in the rejections. Although Applicants believe that there is no teaching or suggestion in the art to use the nucleic acid as a probe to detect nucleic acids encoding Rig and that there in no teaching or suggestion in the art to amplify the

nucleic acid of Lamerdin et al., these points are immaterial in light of the fact that none of the references cited by the Office teach or suggest SEQ ID NO: 5, which is an important element of the rejected claims.

In view of the foregoing arguments, the subject matter of the rejected claims is non-obvious to one of ordinary skill in the art. Therefore, Applicants request that the rejections under Section 103 be withdrawn.

Conclusion

The application is considered to be in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned agent.

Respectfully submitted,

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